

REMARKS/ARGUMENTS

Allowed Claims

Applicants wish to thank the Examiner for indicating that claims 1, 2, 4, 8, and 12-14 are deemed allowable.

35 U.S.C. § 112

It is believed that the crux of the rejection of claim 9 is set forth on page two of the most recent office action:

...the specification only appears to provide examples of treating pain as opposed to preventing pain and it does not appear from the prior art of record that prevention of pain is highly predictable. As such, it appears that one of ordinary skill in the art would be required to do undue experimentation in order to show that the claimed compounds prevent pain.

Applicants respectfully disagree and request that the Examiner consider the following:

The assays described in Example 22 and Example 23 of the application establish a link between the claimed compounds and mGluR5 receptor antagonism. The animal study described in Example 24 establishes that these same compounds have a pain reducing effect. Considered together, these Examples show that mGluR5 receptor antagonism reduces or lessens the current perception of pain.

The claimed compounds will antagonize the mGluR5 receptor independent of whether pain is perceived at a particular moment. It is thus entirely reasonable for the skilled artisan to conclude that a patient, whose mGluR5 receptors are actively being antagonized by a claimed compound, will be prevented from feeling pain (or prevented from feeling as much pain) as a result of future otherwise painful stimuli or conditions. This *preventative* effect will last as long as there is a sufficient degree of mGluR5 antagonism occurring. Put more

simply, as long as mGluR5 receptors are being antagonized, it is reasonable to believe that perception of pain will be prevented.

Applicants take issue with the Examiner's conclusion that "it does not appear from the prior art of record that prevention of pain is highly predictable". The Examiner has cited no teachings in the prior art to support this conclusion. To the contrary, numerous commercial pain remedies are routinely prescribed and effectively used for the *prevention* of the *anticipated* onset of pain. Examples of such remedies include anesthetics for the prevention of pain from surgery, dentistry and childbirth; β -blockers and anti-depressants for the prevention of migraine or cluster headache pain; prophylactic pain medication for reducing the need for post-operative narcotics in children; NSAIDs taken prior to vigorous exercise such as long-distance running or triathlons; and numerous treatments for premenstrual/menstrual pain. Those skilled in the art, for instance medical doctors seeking to prevent the onset of pain symptoms in a patient, are in a position to know when these and other pain symptoms are likely to occur for a particular patient, and regularly prevent this pain.

Further, we reiterate that "prevention" is not understood in the art to mean "that the subject will *never again* suffer pain or that the drug prevents pain *no matter what* the cause". Rather, one skilled in the art would understand (1) that "prevention" relates to those pain conditions wherein the mGluR5 receptor plays a role, and (2) that the duration of the preventative effect would not be unlimited but would be limited by the pharmacological properties of the compound.

Regarding the rejections of claims 15 and 16 for alleged lack of enablement, the Examiner is asked to consider that mGluR5 has been linked to the treatment of these disease conditions in the scientific literature including anxiety and depression,¹⁻⁶ Parkinson's disease,⁷⁻⁹ drug dependence,¹⁰ stroke/brain trauma^{11,12} and mental retardation.¹³ Thus, it is submitted that treatment of the claim 15 and 16 conditions is in fact enabled. (If the Examiner requires copies of any of these references Applicant will provide same upon request.)

Conclusion

In view of the above remarks Applicants respectfully submit that the application is in condition for allowance and request a Notice to that effect. Attorney for Applicants can be reached at the telephone number and address below. Correspondence should be sent to the address below. Any additional fees or deficiency in fees required should be taken from Merck Deposit Account No. 13-2755.

Respectfully submitted,

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